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Congress of the United States

House of Representatives

COMMITTEE ON GOVERNMENT REFORM

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Dr. von Eschenbach :

On September 7, this Subcommittee held a hearing on "Women and Cancer - Where Are We in Prevention, Early Detection and Treatment of Gynecologic Cancers?" Last month, Subcommittee staff informed the FDA that the line of questioning would be similar to that posed to the FDA at a cervical cancer hearing held in March, 2004.[1] Specifically, the Subcommittee staff informed the agency that the Subcommittee would be seeking an explanation about why the FDA has yet to comply with P.L. 106-554, enacted almost five years ago, requiring the FDA to "reexamine existing condom labels...to determine whether the labels are medically accurate regarding the overall effectiveness or lack of effectiveness of condoms in preventing sexually transmitted diseases, including HPV."

The FDA's representative testifying at this hearing was Dr. Richard Pazdur, Director of Office of Oncology Drug Products, Office of New Drugs, in the Center for Drug Evaluation and Research. To the Subcommittee's surprise, Dr. Pazdur's ten-page testimony[2] did not make a single reference to condoms or to the leading cause of cervical cancer, human papillomavirus (HPV), which is transmitted through sexual contact.

In response to the Subcommittee's expressed dissatisfaction with the testimony, the FDA agreed to provide to us within five legislative days of the September 7th hearing an explanation and status report on its long-overdue compliance with P.L. 106-554.

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[1] *Cervical Cancer and Human Papillomavirus, Hearing before the House Subcomm. on Criminal Justice, Drug Policy and Human Resources*, 108th Cong. (2004). Available at http://reform.house.gov/CJDPHR/Hearings/EventSingle.aspx?EventID=11214.

[2] *Women and Cancer – Where Are We in Prevention, Early Detection and Treatment of Gynecologic Cancers? Hearing Before the House Subcomm. on Criminal Justice, Drug Policy, and Human Resources*, 109th Cong. (2005) (Statement of Richard Pazdur, M.D., Director of Office of Oncology Drug Products, Office of New Drugs, in the Center for Drug Evaluation and Research, Food and Drug Administration).

On September 16, we received correspondence from the FDA addressing some of our questions about the FDA's approach to condoms and their lack of effectiveness in preventing the transmission of HPV.[3] It appears that some of the statements within this most recent communication misconstrue the FDA's prior statements on the same subject, and make broad conclusions that extend beyond those reached in prior reports.

Most specifically, the Subcommittee is concerned that the FDA is now more focused on the consequences, rather than the prevention, of HPV infection, and may be giving undue attention to unpublished studies rather than established science.

For instance, the response we received from the FDA on September 16th included the following statement: "In its *Report to Congress: Genital HPV Infection*, CDC considered several more studies and also **concluded** that condom use protects against the most serious consequences of HPV infection" (emphasis added).

However, the actual CDC report to Congress[4] was not so sweeping or conclusive: "Available studies suggest that condoms reduce the risk of the clinically important outcomes of genital warts and cervical cancer... However, all published epidemiologic studies have significant methodologic limitations which make the effect of condoms in prevention of HPV infection unknown....**most studies on genital HPV infection and condom use did not show a protective effect.**"[5]

Contrary to FDA's characterization, the CDC assessment is equivocal, *not* conclusive, about whether condoms reduce the risk of genital warts or cervical cancer. There is substantial danger is promoting a public policy based on uncertain, equivocal information. It would be astounding if the FDA's policy on condom labeling was founded on – at best – uncertainty about condoms' protectiveness against HPV. The only safe policy in such a situation is to err on the side of patient education, not equivocal assurances about uncertain protection.

Moreover, FDA's focus on the *outcomes* of HPV infection does not address the *actual* infection; whether or not someone infected with HPV develops consequential warts or cancer during a given time interval, that person is still infectious and may nevertheless transmit HPV to a sexual partner.

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[3] Letter from Patrick Ronan, Associate Commissioner for Legislation, Food and Drug Administration, to The Honorable Mark Souder, Chairman, Subcomm. on Criminal Justice, Drug Policy and Human Resources (Sept. 16, 2005) (on file with Subcommittee).

[4] Report to Congress: *Prevention of Genital Human Papillomavirus*. Centers for Disease Control and Prevention (January 2004).

[5] Id. at 15.

As the FDA acknowledges, a 2002 meta-analysis[6] of data describing the relationship between condoms and HPV-related conditions found "no consistent evidence of a protective effect of condom use on HPV DNA detection." However, the FDA asserts that "many new studies have been reported" since this meta analysis was published, and concludes that "it is important to view these findings in the context of the clinical outcome of HPV infection."

The FDA's focus on clinical outcome in lieu of prevention is very troubling, and its reference to "many new studies" is unsupported. Even the CDC report references only two studies[7] published since the meta-analysis, and the only study specifically noted by the FDA in its September 16th letter is unpublished.[8]

Dr. von Eschenbach, as I know you are aware, cervical cancer will kill an estimated 3,700 American women this year. More women will die from cervical cancer than HIV/AIDS, among non-injection drug users. The primary cause of cervical cancer is HPV infection. There is no cure for HPV infection, which may also cause genital warts, and may be transmitted to children during childbirth.

Dr. Richard D. Klausner, when he was director of the National Cancer Institute, told Congress that "Condoms are ineffective against HPV because the virus is prevalent not only in the mucosal tissue (genitalia) but also on dry skin of the surrounding abdomen and groin, and it can migrate from those areas into the vagina and the cervix. Additional research efforts by NCI on the effectiveness of condoms in preventing HPV transmission are not warranted."[9]

As far as I am aware, there is no published data to challenge Dr. Klausner's conclusion.

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[6] Manhart, L.E., Koutsky, L.A., *Do condoms prevent gential HPV infection, external genital warts, or cervical neoplasia? A meta-analysis*. Sex Transm. Dis. 2002; 29:725-35.

[7] CDC's report "evaluated 46 peer-reviewed publications in English available after January 1966." The two included studies published after the Manhart and Koutsky meta analysis are (1) Winer, R.L., et al, *Genital human papillomavirus infection: incidence and risk factors in a cohort of female university students*, American Journal of Epidemiology 2003; 157(3):218-226; (2) Hogewoning, C.J., et al, *Condom use promotes regression of cervical intraepithelial neoplasia and clearance of human papillomavirus: a randomized clinical trial*, Int. J. Cancer 107, 811-816. 2003.

[8] Winer, R., et al., *The Effect of Consistent condom Use on the Risk of Genital HPV Infection Among Newly Sexually Active Young Women* (unpublished). This unpublished study was the subject of a letter to you on August 2, 2005 from Congressman Henry A. Waxman, who asked the FDA to consider this unpublished research in the course of its delayed compliance with P.L. 106-554. (Letter from Henry A. Waxman, Ranking Minority Member, Committee on Government Reform, to The Honorable Lester Crawford, Commissioner, Food and Drug Administration (Aug. 2, 2005). Available at http://www.democrats.reform.house.gov/Documents/20050802101833-90561.pdf (last visited September 26, 2005).)

[9] Dr. Richard D. Klausner, Director of the National Cancer Institute, correspondence to U.S. House Commerce Committee, February 19, 1999.

The very serious nature of this disease underscores the necessity for proper labeling of condoms to reflect medically accurate information. I am concerned that the FDA does not share this view, based on its unreasonable delay in complying with PL 106-554, and an apparent shift in focus away from prevention of HPV infection.

Please respond to the following questions no later than 5:00pm Friday, October 7, 2005:

- What studies on the efficacy of condoms to prevent the transmission of HPV, since the Manhart and Koutsky meta-analysis, have been published? Please characterize these studies. Which of them reach the conclusion that condom use reduces the most serious clinical outcomes of HPV infection?

- To what extent has the FDA relied on the unpublished Winer study in its evaluation of condom effectiveness in preventing HPV infection?

- Has the FDA evaluated any peer-reviewed research that would justify a repudiation of the following statement from the CDC's 2004 Report to Congress: "The available scientific evidence is not sufficient to recommend condoms as a primary prevention strategy for the prevention of genital HPV infection?"[10] Please characterize any such research.

Sincerely,

Mark E. Souder
Chairman
Subcommittee on Criminal Justice,
Drug Policy and Human Resources

[10] Report to Congress, supra note 4, at 16.